

WHAT IS CLAIMED IS:

1. An isolated monoclonal antibody that competes for binding to human tau with antibody 3D6.
2. The antibody of claim 1 that binds to the same epitope on human tau as 3D6.
3. The antibody of claim 1, comprising three light chain CDRs as and three heavy chain CDRs of monoclonal antibody 3D6, wherein 3D6 is a mouse antibody characterized by a heavy chain variable region having an amino acid sequence comprising SEQ ID NO: 7 and a light chain variable region having an amino acid sequence comprising SEQ ID NO: 11.
4. The antibody of claim 3, wherein the three heavy chain CDRs are as defined by Kabat/Chothia Composite (SEQ ID NOs: 8, 9, and 10) and the three light chain CDRs are as defined by Kabat/Chothia Composite (SEQ ID NOs: 12, 13, and 14).
5. The antibody of claim 1 that is 3D6 or a chimeric, veneered, or humanized form thereof.
6. The antibody of claim 5, wherein the variable heavy chain has $\geq 85\%$ identity to human sequence.
7. The antibody of claim 5, wherein the variable light chain has $\geq 85\%$ identity to human sequence.
8. The antibody of claim 5, wherein each of the variable heavy chain and variable light chain has $\geq 85\%$ identity to human germline sequence.
9. The antibody of claim 5, wherein the three heavy chain CDRs are as defined by Kabat/Chothia Composite (SEQ ID NOs: 8, 9, and 10) and the three light chain CDRs are as defined by Kabat/Chothia Composite (SEQ ID NOs: 12, 13, and 14); provided that position H27 is occupied by F or Y, H28 is occupied by N or T, H29 is occupied by I or F, H30

is occupied by K or T, position H51 is occupied by I or V, position H54 is occupied by N or D, position H60 is occupied by D or A, H61 is occupied by P or E, and H102 is occupied by F or Y.

10. The antibody of claim 9, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 42.

11. The antibody of claim 9, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 58.

12. The antibody of claim 9, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 59.

13. The antibody of claim 9, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 60.

14. The antibody of claim 9, wherein CDR-H2 has an amino acid sequence comprising SEQ ID NO: 43.

15. The antibody of claim 9, wherein CDR-H2 has an amino acid sequence comprising SEQ ID NO: 61.

16. The antibody of claim 9, wherein CDR-H2 has an amino acid sequence comprising SEQ ID NO: 62.

17. The antibody of claim 9, wherein CDR-H2 has an amino acid sequence comprising SEQ ID NO: 63.

18. The antibody of claim 9, wherein CDR-H2 has an amino acid sequence comprising SEQ ID NO: 64.

19. The antibody of claim 9, wherein CDR-H3 has an amino acid sequence comprising SEQ ID NO: 65.

20. The antibody of any one of the preceding claims, wherein the antibody is a humanized antibody.

21. The humanized antibody of claim 20, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 42 and CDR-H2 has an amino acid sequence comprising SEQ ID NO: 43.

22. The humanized antibody of claim 20, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 42 and CDR-H2 has an amino acid sequence comprising SEQ ID NO:61.

23. The humanized antibody of claim 20, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 42 and CDR-H2 has an amino acid sequence comprising SEQ ID NO:64.

24. The humanized antibody of claim 20, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 42, CDR-H2 has an amino acid sequence comprising SEQ ID NO:63, and CDR-H3 has an amino acid sequence comprising SEQ ID NO:65.

25. The humanized antibody of claim 20, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 58 and CDR-H2 has an amino acid sequence comprising SEQ ID NO:62.

26. The humanized antibody of claim 20, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 59 and CDR-H2 has an amino acid sequence comprising SEQ ID NO:63.

27. The humanized antibody of claim 20, wherein CDR-H1 has an amino acid sequence comprising SEQ ID NO: 60 and CDR-H2 has an amino acid sequence comprising SEQ ID NO:62.

28. The antibody of claim 5, that is a humanized or chimeric 3D6 antibody that specifically binds to human tau, wherein 3D6 is a mouse antibody characterized by a mature heavy chain variable region of SEQ ID NO:7 and a mature light chain variable region of SEQ ID NO: 11.

29. The humanized antibody of claim 28 comprising a humanized mature heavy chain variable region comprising the three heavy chain CDRs of 3D6 and a humanized mature light chain variable region comprising the three light chain CDRs of 3D6.

30. The humanized antibody of claim 29, wherein the CDRs are of a definition selected from the group of Kabat, Chothia, Kabat/Chothia Composite, AbM and Contact.

31. The humanized antibody of claim 30 wherein the humanized mature heavy chain variable region comprises the three Kabat/Chothia Composite heavy chain CDRs of 3D6 (SEQ ID NOs: 8-10) and the humanized mature light chain variable region comprises the three Kabat/Chothia Composite light chain CDRs of 3D6 (SEQ ID NOs: 12-14).

32. The humanized antibody of claim 30 wherein the humanized mature heavy chain variable region comprises the three Kabat heavy chain CDRs of 3D6 (SEQ ID NO:32, SEQ ID NO:9, and SEQ ID NO:10) and the humanized mature light chain variable region comprises the three Kabat light chain CDRs of 3D6 (SEQ ID NOs: 12-14).

33. The humanized antibody of claim 30 wherein the humanized mature heavy chain variable region comprises the three Chothia heavy chain CDRs of 3D6 (SEQ ID NO:33, SEQ ID NO:34, and SEQ ID NO:10) and the humanized mature light chain variable region comprises the three Chothia light chain CDRs of 3D6 (SEQ ID NOs: 12-14).

34. The humanized antibody of claim 30 wherein the humanized mature heavy chain variable region comprises the three AbM heavy chain CDRs of 3D6 (SEQ ID NO:8, SEQ ID NO:35, and SEQ ID NO:10)) and the humanized mature light chain variable region comprises the three AbM light chain CDRs of 3D6 (SEQ ID NOs: 12-14).

35. The humanized antibody of claim 30 wherein the humanized mature heavy chain variable region comprises the three Contact heavy chain CDRs of 3D6 (SEQ ID NOs:39-41) and the humanized mature light chain variable region comprises the three Contact light chain CDRs of 3D6 (SEQ ID NOs:36-38).

36. The humanized antibody of any one of claims 21-35 comprising a humanized mature heavy chain variable region having an amino acid sequence at least 90% identical to any one of SEQ ID NOs:15-19 and SEQ ID NOs:46-57 and a humanized mature light chain variable region having an amino acid sequence at least 90% identical to any one of SEQ ID NOs: 20-23, except that position H17 can be T or S, and position H20 can be I or V.

37. The humanized antibody of claim 36, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H38 is occupied by R and H93 is occupied by S.

38. The humanized antibody of claim 36, provided positions H38 and H93 in the VH region are occupied by R and S, respectively.

39. The humanized antibody of claim 36 wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H38 is occupied by R, H43 is occupied by Q, H83 is occupied by T, and H93 is occupied by S.

40. The humanized antibody of claim 39, provided positions H38, H43, H83, and H93 in the VH region are occupied by R, Q, T, and S, respectively.

41. The humanized antibody of claim 39, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H12 is occupied by V, H24 is occupied by A, H48 is occupied by I, H67 is occupied by A, H80 is occupied by L, H81 is occupied by Q, and H91 is occupied by F.

42. The humanized antibody of claim 41, provided positions H12, H24, H48, H67, H80, H81, and H91 in the VH region are occupied by V, A, I, A, L, Q, and F, respectively.

43. The humanized antibody of claim 41, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H13 is occupied by R and H66 is occupied by K.

44. The humanized antibody of claim 43, provided positions H13 and H66 in the VH region are occupied by R and K, respectively.

45. The humanized antibody of claim 41, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H40 is occupied by R and H82a is occupied by G.

46. The humanized antibody of claim 45, provided positions H40 and H82a in the VH region are occupied by R and G, respectively.

47. The humanized antibody of claim 39, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H42 is occupied by E and H76 is occupied by N.

48. The humanized antibody of claim 47, provided positions H42 and H76 in the VH region are occupied by E and N, respectively.

49. The humanized antibody of claim 37, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H40 is occupied by R, H82a is occupied by G, and H83 is occupied by T.

50. The humanized antibody of claim 49, provided positions H40, H82a, and H83 in the VH region are occupied by R, G, and T, respectively.

51. The humanized antibody of claim 49, wherein H12 in the VH region is occupied by V.

52. The humanized antibody of claim 51, wherein H80 in the VH region is occupied by L.

53. The humanized antibody of claim 52, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H24 is occupied by A, H48 is occupied by I, H67 is occupied by A, H80 is occupied by L, and H91 is occupied by F.

54. The humanized antibody of claim 53, provided positions H24, H48, H67, H80, and H91 in the VH region are occupied by A, I, A, L, and F, respectively.

55. The humanized antibody of claim 52, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H43 is occupied by Q, and H81 is occupied by Q.

56. The humanized antibody of claim 55, provided positions H43 and H81 in the VH region are occupied by Q, and Q, respectively.

57. The humanized antibody of claim 49, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H24 is occupied by A, and H91 is occupied by F.

58. The humanized antibody of claim 57, provided positions H24 and H91 in the VH region are occupied by A and F, respectively.

59. The humanized antibody of claim 57, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H13 is occupied by R, H17 is occupied by L, H29 is occupied by F, H42 is occupied by E, H43 is occupied by Q, H61 is occupied by E, H76 is occupied by N, H80 is occupied by L, H81 is occupied by Q.

60. The humanized antibody of claim 59, provided positions H13, H17, H29, H42, H43, H61, H76, H80, and H81 in the VH region are occupied by R, L, F, E, Q, E, N, L, and Q, respectively.

61. The humanized antibody of claim 51, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H24 is occupied by A, H28 is occupied by T, H48 is occupied by I, H54 is occupied by D, H60 is occupied by A, H67 is occupied by A, H80 is occupied by L, and H91 is occupied by F.

62. The humanized antibody of claim 61, provided positions H24, H28, H48, H54, H60, H67, H80, and H91 in the VH region are occupied by A, T, I, D, A, A, L, and F, respectively.

63. The humanized antibody of claim 51, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H10 is occupied by D,

H17 is occupied by L, H24 is occupied by A, H28 is occupied by T, H43 is occupied by Q, H48 is occupied by I, H60 is occupied by A, H61 is occupied by E, H91 is occupied by F, H108 is occupied by T, and H109 is occupied by L.

64. The humanized antibody of claim 63, provided positions H10, H17, H24, H28, H43, H48, H60, H61, H91, H108, and H109 in the VH region are occupied by D, L, A, T, Q, I, A, E, F, T, and L, respectively.

65. The humanized antibody of claim 52, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H17 is occupied by L, H27 is occupied by Y, H29 is occupied by F, and H61 is occupied by E

66. The humanized antibody of claim 65, provided positions H17, H27, H29, and H61 in the VH region are occupied by L, Y, F, and E, respectively.

67. The humanized antibody of claim 37, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H17 is occupied by L, H27 is occupied by Y, H29 is occupied by F, H61 is occupied by E, H76 is occupied by N, and H82a is occupied by G.

68. The humanized antibody of claim 67, provided positions H17, H27, H29, H61, H76, and H82a in the VH region are occupied by L, Y, F, E, N, and G, respectively.

69. The humanized antibody of claim 37, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H12 is occupied by V, H17 is occupied by L, H24 is occupied by A, H43 is occupied by Q, H48 is occupied by I, H83 is occupied by T, and H91 is occupied by F.

70. The humanized antibody of claim 69, provided positions H12, H17, H24, H43, H48, H83, and H91 in the VH region are occupied by V, L, A, Q, I, T, F, respectively.

71. The humanized antibody of claim 37, wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H12 is occupied by V,

H24 is occupied by A, H48 is occupied by I, H67 is occupied by A, H80 is occupied by L, H83 is occupied by T, and H91 is occupied by F.

72. The humanized antibody of claim 71, provided positions H12, H24, H48, H67, H80, H83, and H91 in the VH region are occupied by V, A, I, A, L, T, and F, respectively.

73. The humanized antibody of claim 36 wherein at least one of the following positions in the VH region is occupied by the amino acid as specified: H10 is occupied by E or D, H12 is occupied by K or V, H13 is occupied by K or R, H17 is occupied by T, L or S, H24 is occupied by V or A, H27 is occupied by F or Y, H28 is occupied by N or T, H29 is occupied by I or F, H30 is occupied by K or T, H38 is occupied by Q or R, H40 is occupied by A or R, H42 is occupied by G or E, H43 is occupied by K or Q, H48 is occupied by M or I, H51 is occupied by V or I, H54 is occupied by N or D, H60 is occupied by D or A, H61 is occupied by P or E, H66 is occupied by R or K, H67 is occupied by V or A, H76 is occupied by D or N, H80 is occupied by M or L, H81 is occupied by E or Q, H82a is occupied by S or G, H83 is occupied by T or R, H91 is occupied by Y or F, H93 is occupied by A or S, H102 is occupied by F or Y, H108 is occupied by T or L, H109 is occupied by L or V.

74. The humanized antibody of claim 73, provided positions H12, H13, H17, H24, H38, H42, H43, H48, H66, H67, H76, H80, H81, H83, H91, and H93 in the VH region are occupied by V, R, L, A, R, E, Q, I, K, A, N, L, Q, T, F, and S, respectively.

75. The humanized antibody of claim 73, provided positions H38, H42, H43, H76, H83, and H93 in the VH region are occupied by R, E, Q, N, T, and S, respectively.

76. The humanized antibody of claim 73, provided positions H12, H13, H17, H24, H38, H40, H42, H43, H48, H66, H67, H76, H80, H81, H82A, H83, H91, and H93 in the VH region are occupied by V, R, L, A, R, R, E, Q, I, K, A, N, L, Q, G, T, F, and S, respectively.

77. The humanized antibody of claim 73, provided positions H12, H24, H38, H40, H43, H48, H67, H80, H81, H82A, H83, H91, and H93 in the VH region are occupied by V, A, R, R, Q, I, A, L, Q, G, T, F, and S, respectively.

78. The humanized antibody of claim 73 provided positions H12, H24, H28, H38, H40, H43, H48, H54, H60, H67, H80, H81, H82A, H83, H91, and H93 in the VH region are occupied by V, A, T, R, R, Q, I, D, A, A, L, Q, G, T, F, and S, respectively.

79. The humanized antibody of claim 73 provided positions H12, H24, H28, H38, H40, H48, H51, H54, H60, H67, H80, H82A, H83, H91, and H93 in the VH region are occupied by V, A, T, R, R, I, V, D, A, A, L, G, T, F, and S, respectively.

80. The humanized antibody of claim 73 provided positions H12, H24, H28, H38, H40, H48, H54, H60, H67, H80, H82A, H83, H91, and H93 in the VH region are occupied by V, A, T, R, R, I, D, A, A, L, G, T, F, and S, respectively.

81. The humanized antibody of claim 73 provided positions H13, H17, H24, H29, H38, H40, H42, H43, H54, H61, H76, H80, H81, H82A, H83, H91, and H93 in the VH region are occupied by R, L, A, F, R, R, E, Q, N, E, N, L, Q, G, T, F, and S, respectively.

82. The humanized antibody of claim 73 provided positions H13, H17, H24, H27, H28, H29, H30, H38, H40, H42, H43, H51, H54, H60, H61, H76, H80, H81, H82A, H83, H91, and H93 in the VH region are occupied by R, L, A, Y, T, F, T, R, R, E, Q, V, D, A, E, N, L, Q, G, T, F, and S, respectively.

83. The humanized antibody of claim 73 provided positions H10, H12, H17, H24, H28, H38, H40, H42, H43, H48, H54, H60, H61, H76, H80, H82A, H83, H91, H93, H108, and H109 in the VH region are occupied by D, V, L, A, T, R, R, E, Q, I, N, A, E, N, L, G, T, F, S, T, and L, respectively.

84. The humanized antibody of claim 73 provided positions H10, H12, H17, H24, H28, H38, H40, H43, H48, H51, H54, H60, H61, H82A, H83, H91, H93, H102, H108, and H109 in the VH region are occupied by D, V, L, A, T, R, R, Q, I, V, D, A, E, G, T, F, S, Y, T, and L, respectively.

85. The humanized antibody of claim 73 provided positions H38 and H93 in the VH region are occupied by R and S, respectively.

86. The humanized antibody of claim 73 provided positions H17, H27, H29, H38, H61, H76, H82A, and H93 in the VH region are occupied by L, Y, F, R, E, N, G, and S, respectively.

87. The humanized antibody of claim 73 provided positions H17, H27, H28, H29, H30, H38, H51, H54, H60, H61, H76, H82A, and H93 in the VH region are occupied by L, Y, T, F, T, R, V, D, A, E, N, G, and S, respectively.

88. The humanized antibody of claim 73 provided positions H12, H38, H40, H48, H66, H67, H76, H80, H82A, H83, and H93 in the VH region are occupied by V, R, R, I, K, A, N, L, G, T, and S, respectively.

89. The humanized antibody of claim 73 provided positions H12, H17, H27, H29, H38, H40, H61, H80, H82A, H83, and H93 in the VH region are occupied by V, L, Y, F, R, R, E, L, G, T, and S, respectively.

90. The humanized antibody of claim 73 provided positions H12, H17, H27, H28, H29, H30, H38, H40, H51, H54, H60, H61, H80, H82A, H83, and H93 in the VH region are occupied by V, L, Y, T, F, T, R, R, V, D, A, E, L, G, T, and S, respectively.

91. The humanized antibody of claim 36, wherein at least one of the following positions in the VL region is occupied by the amino acid as specified: L36 is occupied by L, L37 is occupied by L, and L100 is occupied by G.

92. The humanized antibody of claim 91, provided positions L36, L37, and L100 in the VL region are occupied by L, L, and G, respectively.

93. The humanized antibody of claim 91, wherein at least one of the following positions in the VL region is occupied by the amino acid as specified: L12 is occupied by S and L45 is occupied by K.

94. The humanized antibody of claim 93, provided positions L12 and L45 in the VL region are occupied by S and K, respectively.

95. The humanized antibody of claim 36, wherein at least one of the following positions in the VL region is occupied by the amino acid as specified: L2 is V or I, L7 is S or T, L12 is P or S, L15 is L or I, L36 is L, L37 is L, L45 is R or K, L60 is D or S, L100 is G.

96. The humanized antibody of claim 95, provided positions L12, L36, L37, L45, and L100 in the VL region are occupied by S, L, L, K, and G, respectively.

97. The humanized antibody of claim 95, provided positions L36, L37, and L100 in the VL region are occupied by L, L and G, respectively.

98. The humanized antibody of claim 95, provided positions L36, L37, L60, and L100 in the VL region are occupied by L, L, S, and G, respectively.

99. The humanized antibody of claim 95, provided positions L2, L7, L12, L15, L36, L37, L45, and L100 in the VL region are occupied by I, T, S, I, L, L, K, and G, respectively.

100. The humanized antibody of claim 95, provided positions L2, L7, L12, L15, L36, L37, L45, and L100 in the VL region are occupied by V, S, P, L, L, L, R, and G, respectively.

101. The humanized antibody of claim 36, comprising a mature heavy chain variable region having an amino acid sequence at least 95% identical to any one of SEQ ID NOs:15-19 and SEQ ID NOs:46-57 and a mature light chain variable region having an amino acid sequence at least 95% identical to any one of SEQ ID NOs: 20-23, except that position H17 can be T or S, and position H20 can be I or V.

102. The humanized antibody of claim 101, comprising a mature heavy chain variable region having an amino acid sequence at least 98% identical to any one of SEQ ID NOs:15-19 and SEQ ID NOs:46-57 and a mature light chain variable region having an amino acid sequence at least 98% identical to any one of SEQ ID NOs: 20-23, except that position H17 can be T or S, and position H20 can be I or V.

103. The humanized antibody of claim 102 wherein the mature heavy chain variable region has an amino acid sequence of any of SEQ ID NOs:15-19 and SEQ ID NOs:46-57 and the mature light chain variable region has an amino acid sequence of any one of SEQ ID NO:20-23.

104 The humanized antibody of claim 103 wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:15 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

105. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:15 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

106. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:15 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

107. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:15 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

108. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:16 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

109. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:16 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

110. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:16 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

111. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:16 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

112. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:17 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

113. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:17 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

114. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:17 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

115. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:17 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

116. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:18 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

117. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:18 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

118. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:18 the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

119. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:18 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

120. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:19 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

121. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:19 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

122. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:19 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

123. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:19 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

124. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:46 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

125. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:46 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

126. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:46 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

127. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:46 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

128. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:47 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

129. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:47 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

130. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:47 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

131. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:47 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

132. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:48 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

133. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:48 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

134. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:48 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

135. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:48 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

136. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:49 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

137. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:49 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

138. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:49 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

139. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:49 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

140. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:50 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

141. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:50 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

142. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:50 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

143. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:50 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

144. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:51 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

145. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:51 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

146. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:51 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

147. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:51 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

148. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:52 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

149. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:52 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

150. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:52 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

151. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:52 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

152. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:53 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

153. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:53 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

154. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:53 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

155. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:53 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

156. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:54 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

157. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:54 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

158. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:54 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

159. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:54 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

160. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:55 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

161. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:55 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

162. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:55 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

163. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:55 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

164. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:56 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

165. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:56 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

166. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:56 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

167. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:56 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

168. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:57 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:20.

169. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:57 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:21.

170. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:57 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:22.

171. The humanized antibody of claim 103, wherein the mature heavy chain variable region has an amino acid sequence of SEQ ID NO:57 and the mature light chain variable region has an amino acid sequence of SEQ ID NO:23.

172. The antibody of any one of claims 1-5 wherein the antibody is a chimeric antibody.

173. The antibody of any one of claims 1-5, wherein the antibody is a veneered antibody.

174. The antibody of any one of claims 1-173 that is an intact antibody.

175. The antibody of any one of claims 1-173 that is a binding fragment.

176. The antibody of claim 175, wherein the binding fragment is a single-chain antibody, Fab, or Fab'2 fragment.

177. The antibody of any one of claims 1-173 that is a Fab fragment, or single chain Fv.

178. The antibody of any one of the preceding claims, wherein the isotype is human IgG1.

179. The humanized antibody of any one of claims 28-171 and 173-178 wherein the mature light chain variable region is fused to a light chain constant region and the mature heavy chain variable region is fused to a heavy chain constant region.

180. The humanized antibody of claim 179, wherein the heavy chain constant region is a mutant form of a natural human heavy chain constant region which has reduced binding to a Fc γ receptor relative to the natural human heavy chain constant region.

181. The humanized antibody of claim 179 or 180, wherein the heavy chain constant region is of IgG1 isotype.

182. The antibody of any one of the preceding claims having at least one mutation in the constant region.

183. The antibody of claim 182, wherein the mutation reduces complement fixation or activation by the constant region.

184. The antibody of claim 183 having a mutation at one or more of positions 241, 264, 265, 270, 296, 297, 318, 320, 322, 329 and 331 by EU numbering.

185. The antibody of claim 184 having alanine at positions 318, 320 and 322.

186. The antibody of any one of claims 1-180 wherein the isotype is of human IgG2 or IgG4 isotype.

187. The antibody of any one of claims 1-186, wherein the antibody is at least 95% w/w pure.

188. The antibody of any preceding claim, wherein the antibody is conjugated to a therapeutic, cytotoxic, cytostatic, neurotrophic, or neuroprotective agent.

189. A pharmaceutical composition comprising an antibody as defined in any of claims 1-188 and a pharmaceutically-acceptable carrier.

190. A nucleic acid encoding the heavy chain and/or light chain of an antibody as described in any one of claims 1-189.

191. A recombinant expression vector comprising a nucleic acid of claim 190.

192. A host cell transformed with the recombinant expression vector of claim 191.

193. A method of humanizing a mouse antibody, the method comprising:

(a) selecting one or more acceptor antibodies;

(b) identifying the amino acid residues of the mouse antibody to be retained;

(c) synthesizing a nucleic acid encoding a humanized heavy chain comprising CDRs of the mouse antibody heavy chain and a nucleic acid encoding a humanized light chain comprising CDRs of the mouse antibody light chain; and

(d) expressing the nucleic acids in a host cell to produce a humanized antibody;

wherein the mouse antibody is 3D6, wherein 3D6 is characterized by a mature heavy chain variable region of SEQ ID NO: 7 and a mature light chain variable region of SEQ ID NO:11.

194. A method of producing a humanized, chimeric, or veneered antibody, the method comprising:

(a) culturing cells transformed with nucleic acids encoding the heavy and light chains of the antibody, so that the cells secrete the antibody; and

(b) purifying the antibody from cell culture media;

wherein the antibody is a humanized, chimeric, or veneered form of 3D6.

195. A method of producing a cell line producing a humanized, chimeric, or veneered antibody, the method comprising:

(a) introducing a vector encoding heavy and light chains of an antibody and a selectable marker into cells;

(b) propagating the cells under conditions to select for cells having increased copy number of the vector;

(c) isolating single cells from the selected cells; and

(d) banking cells cloned from a single cell selected based on yield of antibody;

wherein the antibody is a humanized, chimeric, or veneered form of 3D6.

196. The method of claim 195 further comprising propagating the cells under selective conditions and screening for cell lines naturally expressing and secreting at least 100 mg/L/10⁶ cells/24 h.

197. A method of inhibiting or reducing aggregation of tau in a subject having or at risk of developing a tau-mediated amyloidosis, comprising administering to the subject an effective regime of the antibody of any one of claims 1-189, thereby inhibiting or reducing aggregation of tau in the subject.

198. The method of claim 197, wherein the antibody is a humanized version of 3D6.

199. A method of treating or effecting prophylaxis of a tau-related disease in a subject, comprising administering an effective regime of an antibody as defined by any one of claims 1-189 and thereby treating or effecting prophylaxis of the disease.

200. A method of claim 199 wherein the tau-related disease is Alzheimer's disease, Down's syndrome, mild cognitive impairment, primary age-related tauopathy, postencephalitic parkinsonism, posttraumatic dementia or dementia pugilistica, Pick's disease, type C Niemann-Pick disease, supranuclear palsy, frontotemporal dementia, frontotemporal lobar degeneration, argyrophilic grain disease, globular glial tauopathy, amyotrophic lateral sclerosis/parkinsonism dementia complex of Guam, corticobasal degeneration (CBD), dementia with Lewy bodies, Lewy body variant of Alzheimer disease (LBVAD), or progressive supranuclear palsy (PSP).

201. A method of claim 200 wherein the tau-related disease is Alzheimer's disease.

202. The method of claim 201 wherein the patient is an ApoE4 carrier.

203. A method of reducing aberrant transmission of tau comprising administering an effective regime of an antibody as defined in any of claims 1-189 and thereby reducing transmission of tau.

204. A method of inducing phagocytosis of tau comprising administering an effective regime of an antibody as defined in any of claims 1-189 and thereby inducing phagocytosis of tau.

205. A method of inhibiting tau aggregation or deposition comprising administering an effective regime of an antibody as defined in any of claims 1-189 thereby inhibiting tau aggregation or deposition.

206. A method of inhibiting formation of tau tangles comprising administering an effective regime of an antibody as defined in any of claims 1-189.

207. A method of detecting tau protein deposits in a subject having or at risk of a disease associated with tau aggregation or deposition, comprising administering to a subject an antibody defined by any one of claims 1-189, and detecting the antibody bound to tau in the subject.

208. A method of claim 207, wherein the disease associated with tau aggregation or deposition is Alzheimer's disease, Down's syndrome, mild cognitive impairment, primary age-related tauopathy, postencephalitic parkinsonism, posttraumatic dementia or dementia pugilistica, Pick's disease, type C Niemann-Pick disease, supranuclear palsy, frontotemporal dementia, frontotemporal lobar degeneration, argyrophilic grain disease, globular glial tauopathy, amyotrophic lateral sclerosis/parkinsonism dementia complex of Guam, corticobasal degeneration (CBD), dementia with Lewy bodies, Lewy body variant of Alzheimer disease (LBVAD), or progressive supranuclear palsy (PSP).

209. A method of claim 207, wherein the antibody is administered by intravenous injection into the body of the subject.

210. A method of claim 207, wherein the antibody is administered directly to the brain of the subject by intracranial injection or by drilling a hole through the skull of the subject.

211. A method of claim 207, wherein the antibody is labeled.

212. A method of claim 211, wherein the antibody is labeled with a fluorescent label, a paramagnetic label, or a radioactive label.

213. A method of claim 212, wherein the radioactive label is detected using positron emission tomography (PET) or single-photon emission computed tomography (SPECT).

214. A method of measuring efficacy of treatment in a subject being treated for a disease associated with tau aggregation or deposition, comprising

(a) measuring a first level of tau protein deposits in the subject prior to treatment by administering to a subject an antibody defined by any one of claims 1-189, and detecting a first amount of the antibody bound to tau in the subject,

(b) administering the treatment to the subject,

(c) measuring a second level of tau protein deposits in the subject after treatment by administering to a subject the antibody, and detecting the antibody bound to tau in the subject,

wherein a decrease in the level of tau protein deposits indicates a positive response to treatment.

215. A method of measuring efficacy of treatment in a subject being treated for a disease associated with tau aggregation or deposition, comprising

(a) measuring a first level of tau protein deposits in the subject prior to treatment by administering to a subject an antibody defined by any one of claims 1-189, and detecting a first amount of antibody bound to tau in the subject,

(b) administering the treatment to the subject,

(c) measuring a second level of tau protein deposits in the subject after treatment by administering to a subject the antibody, and detecting a second amount of antibody bound to tau in the subject,

wherein no change in the level of tau protein deposits or a small increase in tau protein deposits indicates a positive response to treatment.